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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,109	TEDESCO ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02/10/2009, 03/02/2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37,39-46 and 48-87* is/are pending in the application.

4a) Of the above claim(s) *50-55, 57, 59-71 and 73-76* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37,39-46,48,49,56,58,72 and 77-87* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Technology Center 1600, Art Unit 1644

Applicant's arguments, filed 02/10/2009, have been fully considered but rendered moot in view of the New Grounds of Rejection set forth herein.

2. Applicant's Status Inquiry, filed 03/02/2010, is acknowledged.

This Office Action should serve in response to applicant's Status Inquiry.

The examiner apologizes for any inconvenience to applicant in this matter.

3. Applicant's amendment, filed 02/10/2009, has been entered.
Claims 1-36, 38 and 47 have been canceled.
Claims 37, 39-42, 44-46, 48-49 and 77-78 have been amended.
Claims 80-87 have been added.

Claims 37, 39-46 and 48-87 are pending.

Claims 37, 39-46, 48-49, 56, 58, 72 and 77-87 are under consideration as they read on the elected invention.

Upon reconsideration, claim 72 drawn to kits comprising the anti-C5a antibodies is under consideration as they read on the elected invention.
Applicant should change the status identifier for claim 72 accordingly.

Claims 50-55, 57, 59-71 and 73-76 have been withdrawn as they read on non-elected inventions.

4. Sequence Compliance.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821-1.825. However, this application fails to comply with the requirements set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

The specification describes sequences that do not have the corresponding SEQ ID NOS.

For example, see pages 3, 5, 8, 18 and 19 of the specification.

For example, the Description of the Figures is objected to, given the absence of the appropriate SEQ ID NOS. associated with the sequences described in the drawings.

See 37 CFR 1.821(d) and MPEP 2422.03.

Also, it does not appear that the Sequence Listing provides for the peptide "KSSKC" described on page 3 of the specification.

Applicant is required to fulfill these requirements for sequence compliance.

5. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected. Appropriate corrections are required.

For example, page 4, line 15 of the specification; "compelement" should be "complement".
For example, page 9, line 30 of the specification; "SEQ IDN4" should be "SEQ ID NO: 4".

Trademarks should be capitalized or accompanied by the ® or ™ symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP 608.01.
For example, see pages 11 and 25 of the specification.

6. Claims 37, 39-46, 48-49, 56, 58, 72 and 77-87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 37, 39-46, 48-49, 56, 58, 72 and 77-87 are indefinite in reciting "corresponding to sequence 731-740 of the C5 component of human complement" because the referenced sequence(s) (SEQ ID NO(S)) is (are) not recited.

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. This is a rejection under 35 USC § 112, first paragraph, "written description" (and not new matter).

Claims 81-83, 85-87, 89-91 and 93-94 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

There is insufficient written description encompassing "or a region having at least 80% /95% homology thereto", "allelic variants" and "conservative mutations" as it reads on either the antibodies or the targeted C5a antigen of the claimed invention because the relevant identifying characteristics such as structure of other physical and/or chemical characteristics of "anti-C5a antibody" or "C5a antigen" are not set forth in the specification as-filed, commensurate in scope with the claimed invention.

For example, given the well known high level of polymorphism of immunoglobulins / antibodies, the skilled artisan would not have been in possession of the vast repertoire of antibodies and the unlimited number of antibodies encompassed by the claimed invention; one of skill in the art would conclude that applicant was not in possession of the structural attributes of a representative number of species possessed by the members of the genera of "homologous entities", allelic variants" and "conservative mutant" of the claimed antibodies and /or antigens as indicated above, and broadly encompassed by the claimed invention.

One of skill in the art would conclude that the specification fails to disclose a representative number of species to describe the claimed genera.

It has been well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity, which is characteristic of the parent immunoglobulin. All of the heavy and light chain CDRs should be in their proper order and in the context of framework sequences which maintain their required conformation in order to provide a binding molecule having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites.

Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl Acad Sci USA 79: 1979-1983 (1982).

Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function.

Single amino changes to either a CDR or even in certain circumstances to the framework can result in decrease affinity of antigen or even ablation of antibody binding and specificity.

Also, see the teachings of Colman (Research in Immunology 145: 33-36, 1994) on the effects of amino acid sequence changes on antibody-antigen interactions.

In addition, Kussie et al. (J. Immunol. 152: 146-152, 1994) (e.g., see entire document, including Table I) teach that the substitution Of a single amino acid can totally ablate antigen binding.

Further, Chen et al. (EMBO J., 14: 2784-2794, 1995) teach that the substitution of a single amino acid can totally ablate antigen and that the same substitution in closely related antibodies can have opposite effects binding (e.g., see entire document, including Figure I). For example, the authors compared the effects of identical substitutions in related antibodies DI6 and TI5, and as shown in Figure 3, some substitutions increased antigen binding in one antibody while ablating it in the other.

Also, Lederman et al. (Molecular Immunology 28: 1171-1181, 1991) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document).

In addition, Li et al. (PNAS 77: 3211-3214, 1980) disclose that dissociation of immunoreactivity does not provide sufficient structural and functional characteristics coupled with a known or disclosed correlation between function and structure.

The disclosure fails to describe the common attributes or characteristics that identify members of the genera of "homologous antibodies / antigens", "allelic variants" and conservative mutants.

While the instant specification does disclose the structural aspects of the C5a antigen and certain anti-C5 antibodies,

the instant application has <u>not</u> provided a sufficient description showing possession of the necessary functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genera of "homologous antibodies / antigens", "allelic variants" and conservative mutants", broadly encompassed by the claimed invention.

Further, the Court has interpreted 35 U.S.C. §112, first paragraph, to require the patent specification to "describe the claimed invention so that one skilled in the art can recognize what is claimed. Enzo Biochem, Inc. v. Gen-Probe Inc, 63 USPQ2d 1609 and 1618 (Fed. Cir. 2002). In evaluating whether a patentee has fulfilled this requirement, our standard is that the patent's "disclosure must allow one skilled in the art 'to visualize or recognize the identity of' the subject matter purportedly described." Id. (quoting Regents of Univ. of Cal. v. Eli Lilly & Co., 43 USPQ2d 1398 (Fed Cir. 1997)).

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483.

The Court has held that the disclosure of screening assays and general classes of compounds was not adequate to describe compounds having the desired activity: without disclosure of which peptides, polynucleotides, or small organic molecules have the desired characteristic, the claims failed to meet the description requirement of § 112. See University of Rochester v. G.D. Searle & Co., Inc., 69 USPQ2d 1886,1895 (Fed. Cir. 2004).

The problem here is that the instant specification fails to provide a disclosure of which residues are required for the C5a antigen or anti-C5a antibody to be substantially the same and retain the appropriate antibody specificity for C5a. A skilled artisan cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus that exhibit this functional property.

Therefore, there is insufficient written description for genera of "homologous antibodies / antigens", "allelic variants" and conservative mutants", broadly encompassed by the claimed invention, other than the known C5a antigen and the particular characterized structural elements of the anti-C5a antibodies described in the specification under the written description provision of 35 USC 112, first paragraph.

Applicant is invited to amend the claims to avoid the recitation of "homology", allelic variants" and "conservative mutants" to avoid this rejection.

Applicant is been reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. §§ 102(f) or (g) prior art under 35 U.S.C. § 103(a).

11. Claims 37, 39-40, 56, 58, 72 and 80-83 are rejected under 35 U.S.C. 102(b) as being anticipated or in the alternative are rejected under 35 U.S.C. 103(a) as being unpatentable by Evans et al. (U.S. Patent 6,355,245) (see entire document).

Evans et al. teach C5-specific antibodies, including human antibodies and antigen binding fragments thereof, including single chain antibodies (e.g., see Summary of the Invention and Description of the Preferred Embodiments), including human antibodies (e.g., column 21, paragraphs 5-7), classes of antibodies (see Antibody Engineering) as well as compositions (e.g., see Summary of the Invention) and articles of manufacture (e.g., kits) (e.g., see claims 6-9 on column 25), wherein the antibodies should prevent the cleavage of C5 to form C5a and C5b (e.g., see column 20, paragraph 1) as well as targeting the cleavage site peptide (e.g., see column 21, paragraphs 2-4), as well as the applicability of histidine tag sequences for purification (e.g., see column 24, paragraph 4) (see entire document)

Although Evans et al. does not explicitly teach the amino acid residues 731-740 of C5 per se, Evans et al. clearly teaches targeting the same or nearly the same cleavage site and corresponding properties of antibodies that inhibit the conversion or cleavage of C5.

Since the Office does not have a laboratory to test the reference antibody, it is Applicant's burden to show that the reference antibody does not bind or cross-react with the same cleavage site or epitope.
See In re Best, 195 USPQ 430, 433 (CCPA 1997); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); In re Fitzgerald, 205 USPQ 594 (CCPA 1980).

In the alternative, if the anti-C5 antibodies reduced to practice by Evans et al. do not necessarily bind or cross-react with the same targeted cleavage site / epitopes claimed encompassed in the instant invention,
one of ordinary skill in the art would have been motivated to make such cleavage site-specific antibodies, given the clear teachings of the prior art to target this specific region with the same functional properties of inhibiting C5 cleavage and inflammatory activities taught by Evans et al. and cited herein above.

A recitation of the intended use such as "for mycocardium damage" of the claimed invention (e.g., see claim 58) must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Given the various sources and classes of antibodies engineered for various utilities, one of ordinary skill in the art would have been motivated to provide antibodies of various forms, including chimeric antibodies of different species and classes to meet the needs of the particularly assays or utility as practiced and known at the time the invention was made and consistent with the teachings of the prior art.

12. Claims 37, 39-40, 56, 58, 72 and 80-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al. (U.S. Patent 6,355,245) in view of Lonberg et al. (U.S. Patent No. 5,770,429) (892; of record).

Evans et al. teach C5-specific antibodies, including human antibodies and antigen binding fragments thereof, including single chain antibodies (e.g., see Summary of the Invention and Description of the Preferred Embodiments), including human antibodies (e.g., column 21, paragraphs 5-7), classes of antibodies (see Antibody Engineering) as well as compositions (e.g., see Summary of the Invention) and articles of manufacture (e.g., kits) (e.g., see claims 6-9 on column 25), wherein the antibodies should prevent the cleavage of C5 to form C5a and C5b (e.g., see column 20, paragraph 1) as well as targeting the cleavage site peptide (e.g., see column 21, paragraphs 2-4), as well as the applicability of histidine tag sequences for purification (e.g., see column 24, paragraph 4) (see entire document)

Although Evans et al. does not explicitly teach the amino acid residues 731-740 of C5 per se, Evans et al. clearly teaches targeting the same or nearly the same cleavage site and corresponding properties of antibodies that inhibit the conversion or cleavage of C5.

Lonberg et al. has been added to provide further evidence of the motivation and obviousness of producing human antibodies at the time the invention was made, as evidenced by the following.

"One of the major impediments facing the development of in vivo therapeutic and diagnostic applications for monoclonal antibodies in humans is the intrinsic immunogenicity of non-human immunoglobulins. For example, when immunocompetent human patients are administered therapeutic doses of rodent monoclonal antibodies, the patients produce antibodies against the rodent immunoglobulin sequences; these human anti-mouse antibodies (HAMA) neutralize the therapeutic antibodies and can cause acute toxicity. Hence, it is desirable to produce human immunoglobulins that are reactive with specific human antigens that are promising therapeutic and/or diagnostic targets. However, producing human immunoglobulins that bind specifically with human antigens is problematic" (see column 1, lines 54-67 in particular).

Lonberg et al. teach transgenic mice that, when immunized with an antigen, produce fully human [claims 3, 4] antibodies to that antigen (see entire document).

Given the teachings by Evans on antibodies that target and bind the C5 cleavage site and distinguishing the properties of other anti-C5 antibodies such as the 5G1.1 antibody that does not bind the C5a cleave site (e.g., see Example 13),
one of ordinary skill would have been motivated to generate anti-C5 antibodies that targeted the C5 cleavage site with anti-inflammatory properties.

Given the teachings of Evans et al. and Lonberg et al., it would have been obvious to one of ordinary skill in the art to make human antibodies with various constant regions for various detection, diagnostic and therapeutic utilities with humans, given the decreased immunogenicity and longer half-lives of human antibodies as well as providing the appropriate human immunoglobulin effector functions.

Therefore, it would have obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of Evans et al. and Lonberg et al. to obtain human anti-inflammatory anti-C5 antibodies that targeted the cleavage site of C5. According to Evans et al., a person of ordinary skill in the art would have been motivated to produce such resultant anti-inflammatory anti-C5 antibodies that targeted the cleavage site of C5 for various utilities a anti-inflammatory antibodies. From the teachings of the references, a person of ordinary skill in the art would have a reasonable expectation of success at the time the invention was made. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phillip Gambel/

Primary Examiner
Technology Center 1600
Art Unit 1644
July 6, 2010